REMARKS/ARGUMENTS

Amendments to the Claims

Claims 1, 3 and 4 have been amended by replacing the term "preventing" with the term "treating." Claims 1 and 3 have been amended by replacing the language "of retro-cochlear origin" with "caused by epilepsy." The claim amendments are supported by the present specification, e.g., at page 7, lines 5-6.

Office Action

Withdrawal of the rejection of claims 2 and 3 under 35 U.S.C. § 112, first paragraph, the rejection of claims 1-1 under 35 U.S.C. § 112, second paragraph, the rejection of claims 1-3 under 35 U.S.C. § 103(a), and the restriction as to claim 4 are gratefully acknowledged.

In the present action, claims 1, 3 and 4 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement.

Discussion of the Office Action

In support of the enablement rejection, the Office argues that the specification, while enabling for treating hearing loss in the 4 and 8 kHz tone frequencies associated with epilepsy during 1 hour and the treatment of seizures for up to 80 min, does neither provide enablement for completely preventing epileptic seizures nor for completely preventing hearing loss of retro–cochlear origin. The Office also argues that the specification does not present any study in humans (hearing range from 20 Hz to 20 kHz; Wikipedia, cited by the Examiner) as pointed out by Temkin (D3) for proving antiepileptogenesis effects, and therefore does not support the claimed subject matter.

Applicants respectfully traverse the rejection. The claim amendments are believed to render moot the rejection as it pertains to preventing hearing loss of retro-cochlear origin. Further, Applicants submit that evidence is indeed provided for positive effects against hearing loss caused by epilepsy, as currently claimed. The particular embodiments provided in the Examples of the application should not be considered in a restrictive manner; the findings obtained at 4 and 8 kHz should not be restrictive for the effects or else on other frequencies. Indeed, the trial of all frequencies of the spectrum would have been an

unreasonable amount of work for the inventors, who chose these two frequencies as representative for the whole, as usually referred to in all related publications of the time. At the time of submission of the present application, research of hearing sensitivity was based in the auditory brainstem responses (ABR) elicited by tone bursts within various ranges of frequencies, performed in several animal models. 4 kHz and particularly 8 kHz frequencies were always included in the tested ranges, due to the offered reliability of the technical results. The following works, among others, could serve as references of this procedure:

- Husain K, Scott RB, Whitworth C, Somani SM, Rybak LP, "Dose response of carboplatin-induced hearing loss in rats: antioxidant defense system." Hear Res. (2001) 151: 71-78.
- Laukli E and Mair IW. "Auditory brainstem responses of the cat: on- and off-responses". Audiology (1985) 24:217-226.
- Uzuka Y, Fukaki M, Hara Y, Matsumoto H. "Brainstem auditory evoked responses elicited by tone-burst stimuli in clinically normal dogs." J Vet Intern Med (1998) 12: 22-25.
- McFadden SL, Campo P, Ding D, Quaranta N. "Effects of noise on inferior colliculus evoked potentials and cochlear anatomy in young and aged chinchillas." Hear Res. (1998) 117:81-96.
- McFadden SL, Ding D, Burkard RF, Jiang H, Reaume AG, Flood DG, Salvi RJ. "Cu/Zn SOD deficiency potentiates hearing loss and cochlear pathology in aged 129, CD-1 mice." J Comp Neurol. (1999) 413:101-112
- Alfred C. Coats, MD; James L. Martin, PhD; "Human Auditory Nerve Action Potentials and Brain Stem Evoked Responses effects of Audiogram Shape and Lesion Location." Arch Otolaryngol (1977) 103: 605-622.

Fausti et al. 1991, 1992, were the first to notice that 4 and 8 kHz frequencies are among the gold standards also useful in humans to detect changes in hearing sensitivity:

- Fausti SA, Rappaport BZ, Frey RH, Henry JA, Phillips DS, Mitchell CR, Olson DJ. "Reliability of evoked responses to high-frequency (8-14 kHz) tone bursts." J Am Acad Audiol (1991) 2: 105-114.

- Fausti SA, Frey RH, Henry JA, Olson DJ, Schaffer HI. "Early detection of ototoxicity using high-frequency, tone-burst-evoked auditory brainstem responses." J Am Acad Audiol. (1992) 3: 397-404.

- Norton SJ, Gorga MP, Widen JE, Folsom RC, Sininger Y, Cone-Wesson B, Vohr BR, Mascher K, Fletcher, and Kristin. "Identification of Neonatal Hearing Impairment: Evaluation of Transient Evoked Otoacoustic Emission, Distortion Product Otoacoustic Emission, and Auditory Brain Stem Response Test Performance." Ear & Hearing (2000) 21: 508-528.

All of these authors worked on particular frequencies for their experiments in animal models and in humans, which ought to be assumable all along the corresponding hearing range, as confirmed later in the art.

Indeed, later evolution of the art has confirmed that the provisions made at the filing date of the application are revealed right. Results obtained at the 4 and 8 kHz frequencies render extendable along the hearing spectrum. At this respect, recent results show how vinpocetin improves hearing sensibility at else frequencies, including at 1 kHz (Nekrassov, "B235 Beneficial Effect of Vinpocetin Treatment on Sensorineural Hearing Loss", 2011, Poster at the World Congress of Neuroscience, Florence). Similar results are reported at clinical trials on human patients (Garza-Morales, "Adjunctive Therapy with Vinpocetin in Children with refractory partial Epilepsy: a Pilot Study in Mexico", 2011, Epilepsia 52(6), p352, 23-263).

All of these references support the convenience of considering 4 and 8 kHz frequencies representative, and show that at the filing date of the present application it was consistent to assume the results found therein are applicable for the scope of the animal or human hearing spectrum.

Further, human trials are not necessary in order to establish enablement, and greatly exceed the reasonable expectations that should be required of the inventors. As pointed out by the Examiner, Temkin postulates the need of human experimentation for results on

antiepileptogenesis in a general view; the present application, however, is restricted to the disease's physical outcomes hearing loss and seizures, on which the art has since proven that results obtained on animal experimentation can be overtaken, as mentioned above.

In support of the enablement rejection, the Office additionally argues that the specification does not reasonably provide enablement for completely preventing epileptic seizures for more than 80 min.

Applicants, however, disagree. Based on the acceptance of the Examiner to the subject matter described in the Examples of the present application, i.e., treating of hearing loss in the 4 and 8 kHz tone frequencies during 1 hour and treatment of seizures for up to 80 min, Applicants submit that the said subject matter should also not be restricted after time. Indeed, the "prophylactically administering" feature requires administration before the onset of a seizure and, therefore, already has a time limitation subsumed therein.

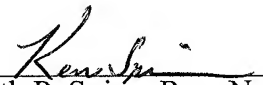
Moreover, it is well within the skill of the ordinarily skilled artisan to modify the time period that the drug remains effective in a particular patient, e.g. by modifying the dose, dosage for (e.g., immediate release, delayed release, etc.) and dosage schedule to maintain therapeutically effective blood levels for any reasonable length of time without undue experimentation, hence, the specification reasonably enables the claimed method. Accordingly, no time restriction should be imposed in view of the preferred embodiments disclosed in the Examples of the application.

For at least the foregoing reasons, Applicants respectfully submit that the amended claims are fully enabled by the specification as filed. Withdrawal of the indefiniteness rejection is therefore respectfully solicited.

Conclusion

Applicants respectfully submit that the present application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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